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Comparison of Angioscopy, Intravascular Ultrasound Imaging and Quantitative Coronary Angiography in Predicting Clinical Outcome After Coronary Intervention in High Risk Patients

STEVEN FELD, MD, MAZEN GANIM, MD, EDGAR S. CARELL, MD, OLLE KJELLGREN, MD, RICHARD L. KIRKEEIDE, PHD, WILLIAM K. VAUGHN, PHD,* RON KELLY, MD, A. IAIN McGHIE, MD, NANCY KRAMER, RN, DAN LOYD, RT, H. VERNON ANDERSON, MD, FACC, GEORGE SCHROTH, MD, FACC, RICHARD W. SMALLING, MD, PHD, FACC

Houston, Texas

Objectives. **The purpose of this study was to identify qualitative or quantitative variables present on angioscopy, intravascular ultrasound imaging or quantitative coronary arteriography that were associated with adverse clinical outcome after coronary intervention in high risk patients.**

Background. **Patients with acute coronary syndromes and complex lesion morphology on angiography are at increased risk for acute complications after coronary angioplasty. Newer devices that primarily remove atheroma have not improved outcome over that of balloon angioplasty. Intravascular imaging can accurately identify intraluminal and intramural histopathologic features not adequately visualized during coronary arteriography and may provide mechanistic insight into the pathogenesis of abrupt closure and restenosis.**

Methods. **Sixty high risk patients with unstable coronary syndromes and complex lesions on angiography underwent angioscopy (n = 40) and intravascular ultrasound imaging (n = 46) during interventional procedures. In 26 patients, both angioscopy and intravascular ultrasound were performed in the same lesion. All patients underwent off-line quantitative coronary arteriography. Coronary interventions included balloon (n = 21) and excimer laser (n = 4) angioplasty, directional (n = 19) and rotational (n = 6) atherectomy and stent implantation (n = 11). Patients were followed up for 1 year for objective evidence of recurrent ischemia.**

Results. **Patients whose clinical presentation included rest angina or acute myocardial infarction or who received thrombolytic therapy within 24 h of procedure were significantly more likely to experience recurrent ischemia after intervention. Plaque rupture or thrombus on preprocedure angioscopy or angioscopic thrombus after intervention were also significantly associated with adverse outcome. Qualitative or quantitative variables on angiography, intravascular ultrasound or off-line quantitative arteriography were not associated with recurrent ischemia on univariate analysis. Multivariate predictors of recurrent ischemia were plaque rupture on preprocedure angioscopy ($p < 0.05$, odds ratio [OR] 10.15) and angioscopic thrombus after intervention ($p < 0.05$, OR 7.26).**

Conclusions. **Angioscopic plaque rupture and thrombus were independently associated with adverse outcome in patients with complex lesions after interventional procedures. These features were not identified by either angiography or intravascular ultrasound.**

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Patients with unstable clinical syndromes and complex lesion morphology are at increased risk for early complications after coronary angioplasty (1,2). Newer interventional devices that primarily remove rather than disrupt atheromatous and thrombotic material obstructing coronary arteries, including directional and rotational atherectomy and excimer laser angioplasty, have not been shown (3–5) to reduce the incidence of restenosis or improve long-term outcome. Intravascular imaging can accurately identify intraluminal and intramural histopathologic features not routinely visualized by standard angiographic techniques (6). Intravascular ultrasound or angioscopy may provide mechanistic insight into the pathogenesis of abrupt closure or restenosis by identifying morphologic features associated with adverse outcome. The purpose of this study was to investigate the relation of qualitative and quantitative findings obtained during angioscopy, intravascular ultrasound imaging or off-line quantitative coronary arteriography on long-term clinical outcome after coronary intervention in high risk patients.

Methods

Study patients. Seventy consecutive high risk patients with unstable clinical presentation and complex lesion morphology on coronary angiography underwent additional intravascular

From the Division of Cardiology, The University of Texas Health Science Center, Hermann Hospital and *Texas Heart Institute, Houston, Texas.

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Address for correspondence: Dr. Richard W. Smalling, University of Texas Medical School, MSB 1.246, 6431 Fannin, Houston, Texas 77030.

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Table 1. Patient Selection

	Patients	
	No.	%
Unstable clinical presentation		
Crescendo angina	26	43
Rest angina	14	24
Recent MI	20	33
Lesion complexity (AHA/ACC)		
A	0	0
B1	4	7
B2	45	75
C	11	18
No. of diseased vessels		
One	44	73
Two	7	12
Three	9	15

AHA/ACC = American Heart Association/American College of Cardiology criteria.

imaging during coronary interventions performed between March 1992 and April 1994. All patients provided written informed consent for the interventional procedure including intravascular imaging, and the protocol was approved by the Institutional Review Board. Sixty patients included in the study group were followed up clinically for 1 year. Of the 10 excluded patients, 7 who were referred for coronary intervention had inadequate follow-up. Three patients did not have successful intravascular imaging of their target lesions. In one of these three, the ultrasound catheter could not be advanced to the site of angioplasty. Two patients (one with angioscopy, one with ultrasound imaging) had suboptimal intravascular imaging of their lesions and were also excluded.

A cohort of 60 patients (mean age ± SD 63 ± 11 years; 65% male) presenting with unstable angina or acute myocardial infarction and predominantly single-vessel complex lesions on coronary angiography were acceptable for final analysis (Table 1). Among the nine patients with three-vessel coronary disease, target lesions were located in saphenous vein grafts in eight and in a native coronary artery in one patient. Target lesions were located in native coronary arteries in 52 patients and in vein grafts in 8. Unstable angina was defined according to the Braunwald classification (7), and patients were classified into two major categories: crescendo angina (class 1) and rest angina (classes 2 and 3).

Angioscopy was performed in 40 patients, in 33 before and in 39 after intervention. Intravascular ultrasound imaging was performed in 46 patients, in 10 before and in 46 after intervention. Twenty-six patients underwent both angioscopy and intravascular ultrasound imaging. In addition to quantitative arteriography performed on-line during the imaging procedure, all patients underwent off-line biplane quantitative coronary arteriography of the target lesion, both before and after coronary intervention, with use of a previously validated system (8). Off-line quantitative coronary arteriography reports were prepared shortly after the procedure by supervised technicians. Detailed evaluation forms for angioscopic and intravascular ultrasound findings were also completed by the operators after these imaging procedures and were subsequently reviewed in blinded manner by experienced investigators. Picture-in-picture technology provided simultaneous intravascular imaging and location of the imaging catheter in relation to the target lesion. Freeze-frame images with on-line measurements and full audio recording during intravascular ultrasound imaging also facilitated comparative review.

Clinical follow-up at 1 year was obtained for all study patients by nurses and physicians unaware of the findings on intravascular imaging. Patients and their referring physicians were contacted and all available medical records including results of exercise electrocardiography, nuclear imaging studies and cardiac catheterization films were reviewed by experts in blinded manner. An adverse outcome after the coronary intervention was defined as the presence of at least one of the following objective indexes of ischemia: 1) cardiac death, 2) nonfatal myocardial infarction, 3) target lesion revascularization by repeat percutaneous coronary intervention or coronary artery bypass surgery, and 4) a positive nuclear imaging study result with a stress-induced reversible myocardial perfusion defect in the region of prior coronary intervention. In addition, for patients with single-vessel coronary disease at the time of intervention, recurrent angina with positive stress test results defined as >1-mm horizontal or downsloping ST segment depression occurring with exercise or in the recovery phase, was also considered evidence for probable target vessel ischemia.

Interventional procedures. Twenty-one patients underwent balloon and 4 excimer laser angioplasty, 19 patients underwent directional and 6 rotational atherectomy and 11 patients underwent stent implantation. Ten patients had primary stenting of nine saphenous vein grafts and one ostial coronary artery lesion with Palmaz or Palmaz-Schatz stents (Johnson & Johnson Interventional Systems). One patient with dissection after angioplasty had a Gianturco-Roubin Flex-Stent (Cook) deployed but was considered in the angioplasty group on an intention to treat basis. Device selection for interventional procedure and intravascular imaging was at the discretion of the operators. Fifty-five of the 60 patients had single-vessel intervention. Four of the other five patients had two-vessel intervention that included a bypass graft, but they underwent intravascular imaging of only one vessel considered the target lesion. In one patient with two-vessel intravascular imaging and intervention, the first intervention was considered to involve the target lesion.

Balloon angioplasty was performed with standard angioplasty techniques by the percutaneous femoral approach with the use of compliant or noncompliant balloons depending on operator preference. Balloons were initially chosen to approximate the size of the reference segment determined by on-line quantitative coronary arteriography. Laser angioplasty was performed by using a xenon chloride excimer laser (CVX-300, Spectranetics) coupled to a 1.4- to 2.0-mm diameter multifiber catheter, operating at a wavelength of 308 nm, repetition rate

of 25 Hz and fluence of 40 to 50 mJ/mm^2 with continuous saline flush. This procedure was followed by adjunctive balloon angioplasty in three patients. Directional coronary atherectomy was performed by using the Simpson Coronary Atherocath (Devices for Vascular Intervention) with the cutting window oriented toward the angiographic site of the lesion. Adjunctive balloon angioplasty was used in 11 of 19 patients at operator discretion; it was guided by on-line quantitative arteriography to optimize results. Rotational atherectomy was performed with the Rotablator (Heart Technology); the final burr size was selected to approximate 80% to 85% of the interpolated diameter of the reference segment. Postprocedure low pressure balloon inflation was employed in four of six patients. Palmaz-Schatz stents were implanted after predilation of the target lesion; and implantation was followed by postdeployment high pressure balloon inflation. A single Gianturco-Roubin stent was deployed for threatened vessel closure accompanying significant dissection after angioplasty.

Coronary imaging. On-line quantitative coronary arteriography using an automated coronary analysis package (Philips Medical System) was used to direct selection of the interventional procedure device. Selected end-diastolic cine frames of simultaneous biplane orthogonal views were digitized for subsequent off-line quantitative arteriographic analysis performed in a blinded manner. Vessel size at the site of and proximal and distal to the lesion, minimal lumen diameter, percent diameter stenosis, stenosis area and stenosis flow reserve were calculated from a computer-generated interpolated reference diameter by using previously validated software for image processing that involves edge detection, contour reconstruction, magnification and pincushion correction and morphologic analysis of the stenosis (8,9). Quantitative arteriography and intravascular imaging were performed after each coronary intervention in nearly all patients. Postprocedure coronary imaging refers to the final lumen appearance after completion of all coronary interventions (atherectomy, angioplasty or stenting).

Angioscopy was performed with a 4.5F ImageCath coronary angioscope (Baxter Healthcare), which is equipped with an occlusive cuff for low pressure inflation proximal to the flush port and a fiberoptic imaging bundle that can extend up to 5 cm into the blood-free field for viewing. The fiberoptic bundle was advanced slowly into the stenosis over a 0.014-in. (0.035 cm) angioplasty guide wire under fluoroscopy while images were recorded on 0.75-in. (1.9-cm) videotape. An attempt was made to cross the lesion, except in the presence of a large protruding thrombus or in the event that resistance was felt and the image indicated that the optical bundle was advancing against tissue. Images were also recorded during slow withdrawal of the fiberoptic bundle. Lesion characteristics included the presence of plaque rupture with obvious disruption of surface morphology, superficial intimal flaps or tissue fronds, deep dissection and thrombus. Plaque color was characterized as either white (gray-white or yellow-white) or yellow (dark yellow or yellow-brown) (10).

Intravascular ultrasound imaging was performed in the majority of patients with a 2.9F Micro View coronary imaging catheter (Cardiovascular Imaging Systems) with a flexible, rotating drive cable and outward-looking 30-MHz ultrasound transducer at the distal tip. Image acquisition was obtained during slow manual withdrawal of the transducer within the catheter body's common lumen under fluoroscopic guidance with intermittent saline flush. Qualitative morphologic features on ultrasonography included lesion calcium (none, arcs of <90°, 90° to 180° or >180°), dissection (minor dissection with a split in the plaque extending to the media and major dissection extending behind the plaque with a clear separation of the plaque from the intima or media), plaque rupture (partial tear without dissection) and mobile thrombus (11). Quantitative measurements included vessel size proximal to, distal to and within the lesion measured from the external elastic lamina to external elastic lamina, minimal lumen diameter, maximal plaque thickness within the lesion and eccentricity index. An eccentric vessel was defined as having a ratio of minimal to maximal plaque thickness <0.5 (11).

Statistical analysis. Results are expressed as mean value ± 1 SD. The unpaired Student *t* test was performed for analysis of continuous variables and the chi-square test or Fisher exact test for categoric data. Stepwise multivariate logistic regression analysis using the SAS system was performed on all variables with a p value <0.07 on univariate analysis or p value < 0.05 considered significant.

Results

Complications. One patient included in the study group had a complication of his imaging procedure. During angioscopy of a mid-right coronary artery stenosis, ventricular fibrillation occurred after cuff inflation in the proximal coronary artery; defibrillation was successful and the patient had no adverse sequelae.

Patient characteristics and outcome. Of the 60 study patients, 17 (28%) had one or more indexes of recurrent ischemia during the year after coronary intervention and were considered to have had an adverse outcome. These included 3 patients with single-vessel coronary disease, angina and positive results on stress electrocardiography, 10 with a newly positive nuclear stress test result, 2 with nonfatal myocardial infarction, and 9 with repeat target lesion revascularization (percutaneous intervention in 5, coronary bypass surgery in 4). Two of 17 adverse events occurred during the immediate coronary intervention period. One patient underwent emergency coronary bypass surgery for abrupt vessel closure and a second had a non-Q wave myocardial infarction with elevation of serum cardiac enzymes after successful stenting of a right coronary graft. No patient died during follow-up. The remaining 43 patients (72%) were event-free during 1 year of follow-up. The presence of recognized cardiac risk factors for coronary artery disease in patients with and without evidence for recurrent ischemia after coronary intervention is shown in Table 2. Patients whose clinical presentation included more

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Table 2. Cardiac Risk Factors and Outcome After Intervention

	No. of Patients	Outcome Group		p Value
		Event Free	Adverse	
Age (yr)		63 ± 12	58 ± 9	0.10
Male	41	28 (68%)	13 (32%)	0.39
Hypertension	35	24 (69%)	11 (31%)	0.53
Diabetes	11	6 (55%)	5 (45%)	0.16
Family history	18	14 (78%)	4 (22%)	0.88
Smoking	25	17 (68%)	8 (32%)	0.26
Hypercholesterolemia	28	16 (57%)	12 (43%)	0.12
Lipid profile				
Total cholesterol		186 ± 43	214 ± 47	0.07
HDL cholesterol		43 ± 17	43 ± 19	0.98
LDL cholesterol		108 ± 30	142 ± 31	0.07
Triglycerides		149 ± 89	155 ± 115	0.87
Clinical presentation				
Crescendo angina	26	25 (96%)	1 (4%)	< 0.001
Rest angina	14	8 (57%)	6 (43%)	
Myocardial infarction	20	10 (50%)	10 (50%)	
Thrombolytic therapy within 24 h	16	7 (44%)	9 (56%)	< 0.02
Total group	60	43 (72%)	17 (28%)	

Data presented are mean value ± SD or number (%) of patients. HDL and LDL = high density and low density lipoprotein, respectively.

unstable coronary syndromes (rest angina and myocardial infarction) were much more likely to experience recurrent ischemia during follow-up than were patients with crescendo angina ($p < 0.001$). Moreover, the administration of thrombolytic therapy (either systemic or intracoronary) within 24 h of interventional procedure was significantly associated with an adverse clinical outcome.

Angiographic characteristics and outcome. Angiographic lesion complexity by American Heart Association/American College of Cardiology (AHA/ACC) classification (12), the presence of calcium or thrombus on angiography and the number of diseased coronary arteries were not predictive of outcome. Patients whose target lesion was located in the saphenous vein graft to the left anterior descending coronary artery were more likely to experience recurrent ischemia ($p = 0.05$) than were patients with other target vessels. However, when all patients with saphenous vein graft interventions were combined, their outcome was not significantly different from that of patients with native coronary artery interventions. Dissection was evident in 27% of patients. Neither the presence nor severity of dissection (National Heart, Lung, and Blood Institute classification [13]) was significantly associated with outcome. The results of off-line quantitative coronary arteriography performed on images obtained before and after

Table 3. Quantitative Coronary Arteriography and Outcome After Intervention

	Patient Group		p Value
	Event Free	Adverse	
Preprocedure (n = 59)			
Proximal diameter (mm)	2.8 ± 0.7	2.4 ± 0.8	0.14
Minimal lumen diameter (mm)	1.0 ± 0.5	0.9 ± 0.4	0.18
Distal diameter (mm)	2.9 ± 0.6	2.6 ± 0.6	0.16
Stenosis area (mm^2)	1.0 ± 0.8	0.8 ± 0.6	0.13
Stenosis length (mm)	13.2 ± 5.5	12.4 ± 7.8	0.68
Percent diameter stenosis	65.8 ± 14.1	66.5 ± 13.7	0.58
Stenosis flow reserve	2.1 ± 1.2	2.1 ± 1.2	0.45
Postprocedure (n = 59)			
Proximal diameter (mm)	3.1 ± 0.7	2.9 ± 0.6	0.36
Minimal lumen diameter (mm)	2.1 ± 0.8	2.1 ± 0.8	0.74
Distal diameter (mm)	2.9 ± 0.8	2.7 ± 0.6	0.94
Stenosis area (mm^2)	3.8 ± 2.9	3.8 ± 2.3	0.73
Percent diameter stenosis	32.5 ± 14.3	28.0 ± 24.3	0.47
Stenosis flow reserve	4.4 ± 0.8	4.4 ± 1.2	0.54

Data presented are mean value ± SD.

Table 4. Postprocedure Intravascular Ultrasound Imaging (n = 45) and Outcome After Intervention

	No. of Patients	Outcome Group		p Value
		Event Free	Adverse	
Minimal lumen diameter		2.9 ± 0.6	2.9 ± 0.4	0.78
Plaque thickness		0.9 ± 0.4	1.0 ± 0.2	0.60
Eccentric lesion	28	21 (75%)	7 (25%)	0.83
Calcium	35	24 (69%)	11 (31%)	0.14
Dissection	15	12 (80%)	3 (20%)	0.51

Data presented are mean value ± SD or number (%) of patients.

coronary intervention in 59 patients and patient outcome are summarized in Table 3. In one patient the off-line quantitative study was not included in the analysis because of suboptimal angiographic imaging of the target lesion. No significant differences were found on quantitative coronary arteriography between event-free patients and those with an adverse clinical outcome.

Intravascular ultrasound findings and outcome. The number of patients who underwent intravascular ultrasound imaging before intervention (10) was too small to obtain meaningful prognostic information. Qualitative and quantitative results of postprocedure intravascular ultrasound imaging and outcome after intervention are summarized in Table 4. Most lesions were eccentric and the presence of calcium and dissection not apparent on angiography were frequently detected by intravascular ultrasound imaging. Of the 35 patients (76%) with calcium present on intravascular ultrasound, 45% had mild (<90°), 26% had moderate (90° to 180°) and 29% had severe (>180°) calcification. On angiography, calcium was clearly present in the arterial wall in <50% of the patients with severe, in 1 patient with moderate and in no patient with either mild or no apparent calcification on intravascular ultrasound. Of the 15 patients (33%) with evidence of dissection on intravascular ultrasound, 53% had minor and 47% had major dissections. Angiography detected dissection that was present on intravascular ultrasound in 60% of patients, whereas intravascular ultrasound detected dissection apparent on angiography in 91% of patients. However, qualitative findings on intravascular ultrasound such as lesion eccentricity, the presence or extent of calcification and the presence or extent of dissection were not associated with clinical outcome (i.e., similar proportions of patients with or without these characteristics had an adverse outcome). The presence of thrombus was not identified on postprocedure intravascular ultrasound imaging. None of the quantitative variables investigated that included linear dimensions of the target vessel and vascular lumen (proximal, distal and site of stenosis) were predictive of clinical outcome. Area measurements of vessel, lumen or plaque were not routinely performed nor recorded prospectively by the operators.

Angioscopic findings and outcome. Yellow plaque was found in 82% of patients on preprocedure angioscopy. Of the six patients (18%) with white or yellow-white plaque, four had crescendo angina, one patient had rest angina and one had an acute myocardial infarction as the presenting symptom (Table 5). None of these six patients had an event during follow-up. Although white plaque was found more frequently in patients with crescendo angina and was associated with a favorable prognosis, the relation of plaque color and either clinical presentation or outcome after intervention did not achieve statistical significance. White plaque also more commonly appeared echogenic on intravascular ultrasound, suggesting that it contained hard, fibrotic material. Among the 20 patients with yellow plaque on angioscopy, the plaque was soft (echolucent) in 11 (55%). Deep dissection was apparent in only three patients, one of whom had recurrent ischemia on nuclear imaging.

Small, mobile intimal flaps were commonly found after coronary intervention and were not associated with adverse

Table 5. Significance of Plaque Color Observed on Preprocedure Angioscopy

	No. of Patients	Plaque Color		p Value
		Yellow	White	
Clinical presentation				0.30
Crescendo angina	13	9 (69%)	4 (31%)	
Rest angina	7	6 (86%)	1 (14%)	
Acute MI	13	12 (92%)	1 (8%)	
Plaque composition on IVUS				0.10
Soft plaque	12	11 (92%)	1 (8%)	
Hard plaque	14	9 (64%)	5 (36%)	
Clinical outcome				0.07
Event-free	22	16 (73%)	6 (27%)	
Adverse	11	11 (100%)	0 (0%)	

Data presented are number (%) of patients. IVUS = intravascular ultrasound imaging; MI = myocardial infarction.

Table 6. Angioscopy and Outcome After Intervention

	No. of Patients	Outcome Group		p Value
		Event Free	Adverse	
Preprocedure (n = 33)				
Plaque rupture	10	3 (30%)	7 (70%)	0.003
Thrombus	13	5 (38%)	8 (62%)	0.006
(+) Urokinase	7	3 (43%)	4 (57%)	1.0
(−) Urokinase	6	2 (33%)	4 (67%)	
Postprocedure (n = 39)				
Intimal flap	27	19 (70%)	8 (30%)	0.68
Thrombus	12	5 (42%)	7 (58%)	0.01

Data presented are number (%) of patients. (−) and (+) Urokinase = intraprocedure urokinase infusion.

outcome (Table 6). Thrombus was present more frequently in patients with rest angina or after acute myocardial infarction than in patients with crescendo angina ($p < 0.05$). The presence of plaque rupture before intervention and thrombus either before or after the procedure was significantly associated with an adverse clinical outcome. Intracoronary urokinase was administered by means of the guiding catheter to 7 of 13 patients with evidence of thrombus on angioscopy before intervention. Six patients receiving intracoronary urokinase had mixed red-white thrombus and one patient had white thrombus present on initial angioscopy. After thrombolytic therapy and interventional procedure, three patients had red-white thrombus, three had white thrombus and one patient did not have thrombus present on postprocedure angioscopy. Of the six patients who did not receive intracoronary thrombolytic therapy, three had red-white thrombus and three had white thrombus present on initial angioscopy. Clinical outcome was similar for the small number of patients who did or did not receive intracoronary urokinase for thrombus present on preprocedure angioscopy.

Predictors of adverse outcome. Univariate and multivariate analyses of variables associated with adverse clinical outcome after coronary intervention are summarized in Table 7. Of the >60 clinical, angiographic, intravascular ultrasound and angioscopic variables examined, the initial variables used in the logistic regression analysis that were significant on univariate analysis with a p value < 0.07 were clinical presentation, use of lytic therapy, target vessel, ACC/AHA lesion classification, preprocedure angioscopic evidence of plaque rupture, preprocedure angioscopic thrombus and postprocedure angioscopic thrombus. On stepwise logistic regression analysis, the presence on angioscopy of either plaque rupture before or thrombus after interventional procedure was independently associated with objective evidence for recurrent ischemia during 1 year of follow-up. In our study, 28% of patients exhibited recurrent ischemia, including 70% of those with preprocedure angioscopic plaque rupture and 58% of those with postprocedure angioscopic thrombus.

Discussion

This was a small, retrospective study of 60 consecutive high risk patients presenting with unstable coronary syndromes and complex lesion morphology who were subjected to intensive investigation with intravascular imaging during interventional procedures. Nearly 50% of the patients studied underwent both angioscopy and intravascular ultrasound imaging. Of patients with native coronary artery intervention, 85% had single-vessel coronary disease, thus facilitating clinical follow-up of their target lesions. Angiographic follow-up was not obtained for the majority of patients who were event-free. Although adjustments for symptomatic status of patients in studies with incomplete angiographic follow-up may be useful in estimating the incidence of restenosis (14), extrapolation based on angiographic findings in patients in this study probably would not provide information beyond that obtained from postprocedure off-line quantitative angiographic measurements and clinical follow-up. Studies involving serial quantitative angiographic and intracoronary echocardiographic measurements have provided predictable relations between "acute gain" after angioplasty or interventions with new devices and "late loss" in coronary lumen diameter as well as mechanistic insight into the process of restenosis (15). However, in a recent analysis of six major trials involving percutaneous intervention (16), there was no correlation between the magnitude of

Table 7. Predictors of Adverse Outcome

	p Value	OR	95% CI
Univariate predictors			
Clinical presentation (rest angina, acute MI)	< 0.001		
Thrombolytic therapy (within 24 h procedure)	< 0.05		
Angioscopic plaque rupture (preprocedure)	< 0.005		
Angioscopic thrombus (preprocedure)	< 0.01		
Angioscopic thrombus (postprocedure)	< 0.05		
Multivariate predictors			
Angioscopic plaque rupture (preprocedure)	< 0.05	10.15	1.41–73.1
Angioscopic thrombus (postprocedure)	< 0.05	7.26	1.05–50.2

CI = confidence interval; OR = odds ratio.

improvement in minimal lumen diameter on angiographic follow-up and clinical outcome. The composite clinical index used in this study to document objective evidence of recurrent ischemia should provide a reliable means for determining the relations among specific findings on intravascular imaging and the biologic response of the target lesion to intervention (17,18).

The major findings of this study were that unstable clinical presentation, including rest angina, myocardial infarction or the recent use of thrombolytic therapy or angioscopic correlates of plaque instability, were significantly associated with recurrent ischemia on univariate analysis. Moreover, the only multivariate predictors of adverse outcome were angioscopic findings of plaque rupture with obvious disruption of surface morphology before intervention or the presence of thrombus. Although significant relations among clinical, angiographic or intravascular imaging findings and outcome present in other studies involving larger numbers of patients may have failed to achieve statistical significance in this study, our findings suggest that clinical or angioscopic correlates of plaque instability are of paramount importance in predicting outcome of coronary interventions. Acute coronary syndromes result from thrombus formation, platelet aggregation and dynamic vasoconstriction at the site of plaque rupture leading to a cyclic alteration of the coronary flow pattern that often heralds temporary or permanent coronary occlusion (19). Local and systemic factors at the time of plaque rupture influence the stability of the growing thrombus, resulting in a clinical spectrum of unstable coronary syndromes (20). On pathologic examination, patients with acute myocardial infarction are significantly more likely to have evidence of plaque rupture and thrombus formation than are patients with either unstable angina or sudden cardiac death. A nonocclusive platelet-rich thrombus was found in 29% of patients with unstable angina, whereas occlusive thrombus containing fibrin was present at autopsy in 69% of patients with fatal acute myocardial infarction (21). In our study, patients with angina at rest or after acute myocardial infarction had thrombus present on angioscopy significantly more frequently than did patients with crescendo angina. Moreover, angiography significantly underestimated the presence of intracoronary thrombus unambiguously identified on angioscopy in this study as a mass protruding into the coronary lumen. Other angioscopic studies (22,23) have also demonstrated a lack of sensitivity in angiography in detecting thrombus that appears adherent to the vessel surface or protrudes into the coronary lumen. The presence of preexisting intracoronary thrombus has consistently been shown (1,2,24) to be among the strongest predictors of unsuccessful angioplasty and abrupt vessel closure. Thrombus formation is the initial response to vascular injury, which promotes cellular recruitment and extracellular matrix deposition leading to restenosis (25).

Although the presence of thrombus portends poor outcome after intervention, we did not find that intracoronary urokinase administered to a small number of nonrandomized patients with angioscopically documented thrombus significantly improved clinical outcome. Preliminary findings in a randomized study of patients with unstable angina and thrombus on angiography (26) suggest that intracoronary urokinase may adversely affect procedure outcome. Because of the high specificity of angiography in identifying thrombus (22,23), intensive investigation of alternative strategies, including the use of specific thrombin inhibitors, platelet antagonists or more effective modes of local delivery of thrombolytic agents, appears practical and warranted (27–29).

Comparative findings during intravascular imaging. Angioscopy was more sensitive than angiography in detecting pathologic features such as plaque rupture, intimal flaps and thrombus present on the lumen surface, but it was insensitive in assessing deep dissection of the arterial wall. Intramural pathologic features were best identified with intravascular ultrasound imaging, which was superior to angiography in determining the presence and extent of vessel calcification and dissection but did not predict outcome. In some studies involving small numbers of patients (30,31), the presence of major dissection on intravascular ultrasound after angioplasty was associated with restenosis. In larger studies including recent prospective trials (32–34), lesion morphology identified by intravascular ultrasound after angioplasty or other percutaneous interventions was not predictive of restenosis or clinical events. None of the quantitative variables investigated in the present study that included linear dimensions of the target vessel were associated with recurrent ischemia. Although not investigated in this study, intravascular ultrasound assessment of residual plaque burden after angioplasty or other transcatheter interventions has been associated with restenosis in some studies (30,32) but not others (31,33).

The precise relation between angioscopic plaque color and composition has not been subject to rigorous investigation. On pathologic examination of atherosclerotic lesions, there is considerable variability in plaque composition among different lesions or within the same lesion. Most plaques contain both hard collagenous and soft atheromatous components, with the former predominating. In unstable coronary syndromes, a significant atheromatous component is usually present (35). On angioscopy, white plaque predominates in restenotic lesions (36) and in stable angina (37), whereas yellow plaque is more common in unstable coronary syndromes (38,39). Itoh et al. (37) reported that patients with stable angina and white plaque on angioscopy were more prone to experience restenosis after angioplasty. In a single patient evaluated by angioscopy and intravascular ultrasound, white plaque appeared echogenic, supporting clinical suspicion that white plaque contains hard, fibrous tissue, whereas yellow plaque is composed of soft, atheromatous material (37). In our study, 26 patients underwent both angioscopy and intravascular ultrasound imaging. We found that among the 20 patients with yellow plaque on angioscopy, the plaque was soft (echolucent) in 11 (55%). Among the six patients with white plaque, the plaque was hard (echogenic) in five (83%). In our patients with unstable coronary syndromes, the presence of white plaque on angioscopy tended to be associated with a favorable prognosis

($p < 0.07$), which is concordant with data recently reported by Bauters et al. (40).

Both intravascular imaging procedures performed after coronary intervention were frequently followed by subsequent coronary interventions including repeat or adjunctive angioplasty, larger device size or new device, or the use of intracoronary thrombolytic therapy. Twenty patients (51%) with postprocedure angioscopy had further intervention, whereas 18 (39%) with intravascular ultrasound imaging after an interventional procedure required subsequent intervention. The impact of further intervention on outcome as assessed by findings on postprocedure intravascular imaging cannot be ascertained from this study because there was no control group.

Limitations of the study. Although most information obtained from intravascular imaging was prospectively recorded, the study design was retrospective with inherent preselection bias in terms of device selection for interventional procedures and intravascular imaging. Accordingly, there were no predetermined protocols for patient evaluation after procedure to ensure uniform clinical follow-up. Coronary arteriography was not routinely performed in all patients at late follow-up after their procedure and may have provided complementary information about the relation between findings on intravascular imaging and target lesion response to intervention. Significant relations among clinical, angiographic or intravascular imaging findings and outcome may not be evident in this study because of the small sample size.

Conclusions. In a consecutive series of high risk patients with unstable coronary syndromes and unfavorable lesion morphology subjected to angioscopy, intravascular ultrasound, or both intravascular imaging modalities, plaque rupture and thrombus present on angioscopy were independent predictors of adverse clinical outcome during 1 year of follow-up.

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